## GHERARDi et al Serial No. 09/423,516

the same are attached. Nothing further is believed to be required in response to the Office Action of June 27, 2001, however the Examiner is requested to contact the undersigned if otherwise.

Respectfully submitted,

**NIXON & VANDERHYE P.C.** 

Bv:

**B. J. Sadoff** Reg. No. **36,663** 

**BJS:eaw** 

1100 North Glebe Road, 8th Floor Arlington, VA 22201-4714

Telephone: (703) 816-4000 Facsimile: (703) 816-4100

## MARKED UP PAGES OF SPECIFICATION

Page 30, delete lines 1 through 10:

[Figure 7 shows the amino acid sequence of human hepatocyte growth factor from the Swiss Prot database accession no. P14210. Nucleotide sequences encoding HGF or information relating to such sequences are given in Seki *et al* (1991) *Gene* **102**, 213-219; Miyazawaka *et al* (1989) *Biochem. Biophys. Res. Comm.* **163**, 967-973; Seki *et al* (1990) *Biochem. Biophys. Res. Comm.* **172**, 321-327; Nakamura *et al* (1989) *Nature* **342**, 440-443; Weidner *et al* (1991) *Proc. Natl. Acad. Sci. USA* **88**, 7001-7005; Yushiyama *et al* (1991) *Biochem. Biophys. Res. Comm.* **175**, 660-667; and Lokker *et al* (1992) *EMBO J.* **11**, *2503-25* 10 all of which are incorporated herein by reference.] and insert the following therefor:

-- Figure 7 (SEQ ID NO:2) shows the amino acid sequence of human hepatocyte growth factor from the Swiss Prot database accession no. P14210. Nucleotide sequences encoding HGF or information relating to such sequences are given in Seki *et al* (1991) *Gene* **102**, 213-219; Miyazawaka *et al* (1989) *Biochem. Biophys. Res. Comm.* **163**, 967-973; Seki *et al* (1990) *Biochem. Biophys. Res. Comm.* **172**, 321-327; Nakamura *et al* (1989) *Nature* **342**, 440-443; Weidner *et al* (1991) *Proc. Natl. Acad. Sci. USA* **88**, 7001-7005; Yushiyama *et al* (1991) *Biochem. Biophys. Res. Comm.* **175**, 660-667; and Lokker *et al* (1992) *EMBO J.* **11**, *2503-25* 10 all of which are incorporated herein by reference.--

Page 32, delete lines 6 through 20

[In vitro mutagenesis of the hairpin structure and kringle 2

A double stranded oligonucleotide (5'-CA CAG TCA GGA CAT CAT CAT CAT CAT CAT CAT CAT TAA GGA TCC TCT AGA GGT AC -3') coding for six histidine residues and a stop codon was cloned into the Kpn I restriction site of the 2.2 kb Bam HI/Kpn I fragment of the HGF/SF cDNA. In initial experiments, a cDNA encoding wt- HGF/SF fused to a C-terminal. heamagglutinin tag was used (26). For the generation of point mutants of the hairpin structure or kringle 2, codon substitutions were introduced into the cDNA by annealing mismatched primers in PCR reactions. The PCR fragments were cloned into the cDNA and mutations confirmed by sequencing. The point mutants generated in this way are listed in the legend to Fig. 1. For deletion of the hairpin structure, an additional Pst I restriction site was created at nt 300 and, by partial digestion, a fragment coding for amino acids 68 to 100 of HGF/SF was deleted.]

and insert the following therefor:

--In vitro mutagenesis of the hairpin structure and kringle 2

A double stranded oligonucleotide (5'-CA CAG TCA GGA CAT CAT CAT CAT CAT CAT CAT TAA GGA TCC TCT AGA GGT AC -3') (SEQ ID NO:1) coding for six histidine residues and a stop codon was cloned into the Kpn I restriction site of the 2.2 kb Bam HI/Kpn I fragment of the HGF/SF cDNA. In initial experiments, a cDNA encoding wt-HGF/SF fused to a C-terminal. heamagglutinin tag was used (26). For the generation of point mutants of the hairpin structure or kringle 2, codon substitutions were introduced into the cDNA by annealing mismatched primers in PCR reactions. The PCR fragments were cloned into the cDNA and mutations confirmed by sequencing. The point mutants generated in this way are listed in the legend to Fig. 1. For deletion of the hairpin

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structure, an additional Pst I restriction site was created at nt 300 and, by partial digestion, a fragment coding for amino acids 68 to 100 of HGF/SF was deleted.--